

Examiner cited the Cahalan patent for disclosing a crosslinking agent for attaching a growth factor biomolecule to a spacer attached to a substrate. Applicants have amended claim 1 to more particularly point out their claimed invention. Applicants respectfully request reconsideration of the rejection over the Cahalan patent based on the following comments.

As amended, claim 1 recites that the substrate is selected from the group consisting of heart valves, aortic roots, aortic walls, aortic leaflets, pericardial tissue, submucosa and resorbable polymers. The Cahalan patent does not disclose the claimed substrates. Therefore, the Cahalan patent does not anticipate Applicants' presently claimed invention.

Applicants respectfully request withdrawal of the rejection of claims 1, 3, 4, 8, 9, 11, 12 and 15 under 35 U.S.C. §102(b) as being anticipated by the Cahalan patent.

Rejections Over Rodman

The Examiner rejected claim 28 under 35 U.S.C. §102(b) as being anticipated by U.S. Patent 5,606,026 to Rodman (the Rodman patent). The Examiner asserted that the Rodman patent anticipates the claims wherein 2 mm strips described in the Rodman patent are the substrates as claimed. Applicants maintain that the Rodman patent does not disclose Applicants' claimed invention. To clarify the scope of the invention, Applicants have amended claim 28. Applicants respectfully request reconsideration of the rejection over the Rodman patent based on the following comments.

A claim is anticipated only if "each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *In re Robertson*, 49 USPQ2d 1949, 1950 (Fed. Cir. 1999), citing *Verdagaal Bros., Inc. v. Union Oil Co.*, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). Claim 28 recites a prosthesis. To clarify the scope of the claim, Applicants amended claim 28 to note explicitly that the substrate is biocompatible. The Rodman patent does not disclose prostheses having biocompatible substrates with the Tat

protein. In contrast, the Rodman patent discloses assays to evaluate antibody bonding to Tat proteins. See column 16, lines 28-39. Since the Rodman patent does not disclose prostheses, the Rodman patent does not anticipate claim 28.

Applicants respectfully request withdrawal of the rejection of claim 28 under 35 U.S.C. §102(b) as being anticipated by the Rodman patent.

Rejection Over Cahalan et al. and Goldstein

The Examiner rejected claim 10 under 35 U.S.C. §103(a) as being unpatentable over the Cahalan patent in view of U.S. Patent 5,613,982 to Goldstein (the Goldstein patent). The Examiner cited the Goldstein patent for disclosing the use of porcine tissue "for similar implants" as in the Cahalan patent. Applicants believe that the combination suggested by the Examiner does not follow from the cited references. Applicants respectfully request reconsideration of the rejection based on the following comments.

"[O]bviousness cannot be established by combining the teachings of the prior art to produce the claimed invention, absent some teaching, suggestion or incentive supporting the combination." In re Bond, 15 USPQ2d 1566, 1568 (Fed. Cir. 1990)(quoting Carella v. Starlight Archery and Pro Line Co., 231 USPQ 644, 647 (Fed. Cir. 1986)). "[T]he mere fact that the prior art could be so modified would not have made the modification obvious unless the prior art suggested the desirability of the modification." In re Laskowski, 10 USPQ2d 1397, 1398 (Fed. Cir. 1989)(quoting In re Gordon, 221 USPQ 1125, 1127 (Fed. Cir. 1984).

The Cahalan patent describes the "enhancement of biocompatibility of surfaces by binding biomolecules to the surface." See column 1, lines 5-7. An "important aspect" of the Goldstein embodiments is "that the decellularized transplant tissue matrix may be repopulated with cells in vitro." See column 9, lines 34-36 and throughout the Goldstein patent. Growth factors may be added to the growth medium to enhance cell chemotaxis. See column 9, lines 49-

62 and column 10, lines 11-18. Since the Goldstein patent discloses the addition of growth factors dissolved within a cell culture medium for incubation with cells to repopulate the tissue matrix, there would be no motivation also to bind the growth factors to the surface. Therefore, the combined disclosures of the Cahalan patent and the Goldstein patent do not lead to Applicants' claimed invention. Since the references do not lead to Applicants' claimed invention, the combined disclosures of the Cahalan patent and the Goldstein patent do not render the claimed invention obvious.

Applicants respectfully request withdrawal of the rejection of claim 10 under 35 U.S.C. §103(a) as being unpatentable over the Cahalan patent in view of U.S. Patent 5,613,982 to Goldstein (the Goldstein patent).

Rejections Over Cahalan et al and Robertson et al.

The Examiner rejected claim 17 under 35 U.S.C. §103(a) as being unpatentable over the Cahalan patent in view of U.S. Patent 3,755,042 to Robertson et al. (the Robertson patent). The Examiner cited the Robertson patent for disclosing sterilizing and packaging medical articles. Applicants respectfully request reconsideration of the rejection over the Cahalan patent and the Robertson patent.

As noted above, the Cahalan patent does not teach or suggest the substrates recited in Applicants' amended claim. Similarly, the Robertson patent does not teach or suggest the substrate being selected from the group consisting of heart valves, aortic roots, aortic walls, aortic leaflets, pericardial tissue, submucosa and bioresorbable polymers. Since the cited references do not teach or suggest the claimed biocompatible materials, the combined disclosures of the Cahalan patent and the Robertson patent do not render Applicants' claimed invention obvious.

Applicants respectfully request withdrawal of the rejection of claim 17 under 35 U.S.C. §103(a) as being unpatentable over the Cahalan patent in view of the Robertson patent.

Rejections Over Cahalan et al. and Bayne et al.

The Examiner rejected claims 13 and 16 under 35 U.S.C. §103(a) as being unpatentable over the Cahalan patent in view of European application EP 0476983 to Bayne et al. (the Bayne EP application). The Examiner cited the Bayne EP application for disclosing VEGF and the culturing of cells onto the implant. Applicants respectfully request reconsideration of the rejection based on the following comments.

The Bayne EP application, like to the Cahalan patent, does not teach or suggest substrates selected from the group consisting of heart valves, aortic roots, aortic walls, aortic leaflets, pericardial tissue, submucosa and resorbable polymers. Claim 1 has been amended to indicate that the substrate is selected from the group consisting of heart valves, aortic roots, aortic walls, aortic leaflets, pericardial tissue, submucosa and resorbable polymers. Since the cited references do not teach or suggest this feature of the claimed invention, the combined disclosures of the Cahalan patent and the Bayne EP application does not render the claimed invention obvious.

Applicants respectfully request withdrawal of the rejection of claims 13 and 16 under 35 U.S.C. §103(a) as being unpatentable over the Cahalan patent in view of the Bayne EP application.

CONCLUSIONS

In view of the foregoing, it is submitted that this application is in condition for allowance. Favorable consideration and prompt allowance of the application are respectfully requested.

The Examiner is invited to telephone the undersigned if the Examiner believes it would be useful to advance prosecution.

Respectfully submitted,



Peter S. Dardi, Ph.D.
Registration No. 39,650

Customer No. 24113
Patterson, Thunte, Skaar & Christensen, P.A.
4800 IDS Center
80 South 8th Street
Minneapolis, Minnesota 55402-2100
Telephone: (612) 349-5746

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Peter S. Dardi

ATTACHMENT
MARKED-UP AMENDMENT

Specification As Amended

At page 21, line 23 to page 22, line 2, the paragraph has been amended as follows:

In certain preferred embodiments, the polyvalent cations are associated with only a portion of the substrate. In particular, for tissue heart valves, it may be desirable to only associate the ions with the valve wall, such as the aortic wall for an aortic valve, while leaving the leaflets untreated with the ions. The entire tissue valve preferably would be treated with the VEGF. The treatment of only a portion of a [prosthesis] prosthesis with a solution, such as a solution containing polyvalent cations, is described further in copending and commonly assigned U.S. Patent Application Serial No. [08\850.812] 08/850,812, now U.S. Patent 6,206,917 to Williams et al., entitled "Differential Treatment of Prosthetic Devices," incorporated herein by reference.

At page 22, lines 3-21, the paragraph has been amended as follows:

Alternatively, the polyvalent ions can be associated with exogenous storage structures which are in turn associated with the substrate. The use of exogenous storage structures for the storage of anticalcification metal ions is described in copending, commonly assigned patent applications Serial Nos. 08/595,402, now U.S. Patent 6,193,749, and 08/690,661, now U.S. Patent 6,302,909, both incorporated herein by reference. Similarly, certain metals such as silver have been associated with antimicrobial activity. Exogenous storage structures can be used to store suitable antimicrobial metal ions in association with a substrate as described in copending and commonly assigned patent application Serial No. 08/787,139, now U.S. Patent 6,013,106, incorporated herein by reference. Preferred exogenous storage structures include, for example, ferritin and other metal

storage proteins. The exogenous storage proteins can be associated with the substrate in ways similar to those used for VEGF. The activities should not interfere with each other.

Claims As Amended

Claims 1 and 28 have been amended as follows:

1. (Five Times Amended) A prosthesis comprising a substrate and a polypeptide growth factor associated with the substrate by covalent bonding using crosslinking agents, antibody-antigen associations, specific binding protein-receptor associations or enzyme-substrate associations, wherein the crosslinking agents comprise at least two aldehyde functional groups that form covalent bonds to link the crosslinking agent with the polypeptide growth factor and the substrate, the polypeptide growth factor associated with the substrate being effective to stimulate association of viable cells with the substrate, and the substrate being selected from the group consisting of heart valves, aortic roots, aortic walls, aortic leaflets, pericardial tissue, submucosa and bioresorbable polymers.

28. (Amended) A prosthesis comprising a biocompatible substrate and a polypeptide growth factor associated with the biocompatible substrate, the polypeptide growth factor being effective to stimulate association of viable cells with the substrate, wherein the polypeptide growth factor comprises Tat protein.